

**REMARKS**

Applicants affirm the election, without traverse, to prosecute claims 1-14. The Group II claims have been canceled without prejudice to their being submitted as a part of a divisional application. The Group III claims have been amended so as to incorporate all of the limitations of claim 1 and are being retained as presently withdrawn. Upon allowance of claim 1, it is submitted that, under the present USPTO procedures established for this biotechnological art, such claims to a process for using a product should be rejoined therewith. New claims 23-25 are patterned after original claim 11 and recite more of the details illustrated in FIGS. 1, 2 and 3; they are submitted herewith for consideration as drawn to the elected invention.

The Examiner's objection to various of the claims under 35 USC § 112, second paragraph, have been considered, and semantic changes have been made to the claims to obviate these formal objections. Reconsideration of the amended claims and withdrawal of the rejection under 35 USC § 112, second paragraph, are respectfully requested.

Claim 1, as amended, would not be anticipated by the disclosure in the 1995-1996 Sigma-Aldrich Techware Catalog, page 181 which merely illustrates some "shake flasks" which, as best as can be determined, merely interrupt the otherwise smooth interior character of the circular glass wall of a flask to create some baffles that would facilitate mixing. The illustrated flasks are in no way concerned with fragmenting bubbles, and such a flask would be singularly unsuitable for supporting a microarray. The rounded indentations in the glass would not fracture any bubbles which, if present, would merely escape via the upper surface. It is submitted that claim 1 contains recitations which clearly distinguish it from this incidental disclosure of a one piece, glass flask.

Amended claim 1 would not be obvious from the disclosure of U.S. Patent No. 6,186,659 to Schembri (hereinafter Schembri) when taken in combination with the disclosure of U.S. Patent Application Publication No. 2003/0123322 to Chung et al. (hereinafter Chung et al.). Schembri discloses a device for mixing a film of fluid by using a plurality of heat sources, such as resistance heaters, to nucleate (form) bubbles in the film of liquid and create movement of those bubbles in the liquid as a result of thermocapillary action to effect swirling and mixing (see column 5, lines 39-42). This method of mixing is clearly in contrast to Applicants' fracturing bubbles by rupturing them into a plurality of microbubbles as a result of the presence of a plurality of bubble-fracturing elements that extend inwardly from a generally perpendicular surface of a border frame. Schembri proposed to create bubbles by heating a liquid within a chamber that has a smooth, circular outer wall to effect mixing flow along that circular periphery.

The secondary reference, Chung et al. shows two different devices that can be independently incorporated into a microelectromechanical system (MEMS) product, i.e. a mixer (shown in FIGS. 1 and 2) and a reactor (shown in FIGS. 3, 4 and 5). The mixer employs a smooth-walled interior chamber into which two fluids to be mixed are continuously injected tangentially so that they mix with each other and exit in a direction perpendicular to the plane of entry by following a spiral flow pattern through an upper outlet 14. Rather than focus upon the mixer, the Examiner directs attention to the reactor illustrated in FIGS. 3, 4 and 5 (see heading and paragraph 0045). The reactor is unconcerned with mixing; it envisions continuous flow through a microfluidic device, i.e. through three elongated channels defined by two baffles in the form of rectangular parallelpipedes. The purpose of the baffles, as clearly set forth in paragraph 0056, is

merely to provide a surface for immobilization thereon of a “sorptive material” which will separate the sample material of interest from the liquid being caused to flow therethrough. The arrangement of this reactor clearly has no concern with fragmenting bubbles, nor with causing mixing movement of a confined liquid to distribute such effectively across an entire microarray. The mere inclusion of two rectangular parallelepiped baffles in the interior of a chamber within a microfluidic device through which liquid is continuously pumped is submitted to have no reasonable relationship to a peripheral barrier which borders a chamber and has surfaces formed with a plurality of bubble-fracturing elements that will fracture a bubble initially present in a confined body of liquid in the chamber by causing bubbles to rupture upon manipulation of the device. Moreover, the Chung et al. device is not intended to be in any way manipulated; it is simply retained in one position while liquid is pumped therethrough.

In addition to the foregoing structural deficiencies, it is submitted that the Examiner has failed to establish a *prima facie* case for the combination of the Chung et al. description of a reactor for separating a component from a liquid solution, and the Schembri device for heating the exterior circular periphery of a liquid-containing device to cause formation of bubbles from that liquid and the consequent movement of that liquid as a result of thermocapillary action.

With respect to the rejection under 35 U.S.C. § 103, in proceedings before the USPTO, the Examiner bears the burden of establishing a *prima facie* case of obviousness based upon the prior art. The Examiner can satisfy this burden only by showing some objective teaching in the prior art that would lead an individual to combine the relevant teachings of the references. It is submitted that there is no objective teaching in either of

these references that would suggest or motivate one to combine the two teachings to arrive at Applicants' claimed invention.

The Federal Circuit has often reiterated the manner in which obviousness rejections are to be reviewed. Where claimed subject matter has been rejected as obvious in view of a combination of prior art references, "a proper analysis under § 103 requires, *inter alia*, consideration of two factors: (1) whether the prior art would have suggested to those of ordinary skill in the art that they should make the claimed composition or device, or carry out the claimed process; and (2) whether the prior art would also have revealed that in so making or carrying out, those of ordinary skill would have a reasonable expectation of success." *In re Vaeck*, 947 F.2d 488, 493, 20 U.S.P.Q.2d 1438, 1442 (Fed. Cir. 1991), citing *In re Dow Chemical Co.*, 837 F.2d 469, 473, 5 U.S.P.Q.2d 1529, 1531 (Fed. Cir. 1988). The Federal Circuit emphasized this holding by succinctly summarizing: "Both the suggestion and the reasonable expectation of success must be founded in the prior art, not in the Applicants' disclosure" *Id.*

It is settled law that the combination of one reference with another is not proper unless there is some suggestion or motivation to make such a modification -- which may not be only in the hindsight of Applicants' disclosure. In this respect, the decision of the CAFC in the case of *In re Fritch*, 23 USPQ2d 1780, 1783 (Fed. Cir. 1992) is particularly pertinent:

"Obviousness cannot be established by combining the teachings of the prior art to produce the claimed invention, absent some teaching or suggestion supporting the combination. Under section 103, teachings of references can be combined only if there is some suggestion or incentive to do so. *ACS Hosp. Systems, Inc. v. Montefiore Hosp.*, 732 F.2d 1572, 1577, 221 USPQ 929, 933 (Fed. Cir. 1984). Although couched in terms of combining teachings found in the prior art, the same inquiry must be carried out in the context of a purported obvious 'modification' of the prior art. The mere fact that the prior art may be modified in the manner

suggested by the Examiner does not make the modification obvious unless the prior art suggested the desirability of the modification."

In summary, the Examiner has the burden to make a *prima facie* case of obviousness, and such a *prima facie* case requires teaching or suggestion which supports the combination in one of the prior art references. Absent such, the *prima facie* case fails. The Federal Circuit has stated that

"...rejections on obviousness grounds cannot be sustained by mere conclusory statements; instead, there must be some articulated reasoning with some rational underpinning to support the legal conclusion of obviousness." *In re Kotzab*, 217 F.3d 1365, 1370 [55 USPQ2d 1313] (Fed. Cir. 2000).

In that decision, the Federal Court stated "Broad conclusory statements standing alone are not 'evidence'" *Id.* and held that:

"In light of our holding of the absence of a motivation to combine the teachings in Evans, we conclude that the Board did not make out a proper *prima facie* case of obviousness...." *Id.*

It is submitted that the Examiner has not here made any such reasonable showing supported by articulated reasoning with rational underpinnings, and it is submitted such a showing is simply incapable of being made.

Accordingly, reconsideration of amended claim 1 and dependent claims 2-10 and allowance of these claims over the disclosures of Schembri and Chung et al. by withdrawal of their rejection on such combination of references are respectfully requested. Independent claims 11 and 23, for the reasons as are set forth above, are submitted to be similarly unobvious over the asserted combination of Schembri and Chung et al.

Applicants invention as defined in claim 6 which recites the disposition of a plurality of generally triangular fingers which project from two opposed boundary walls, which fingers have sharp edges at their tips and pockets located therebetween further distinguishes from the disclosures of Schembri and Chung et al. and the additional disclosure of U.S. Patent No. 4,750,556 to del Valle P. et al. (hereinafter del Valle et al.). Del Valle et al. teaches a reactor apparatus wherein mixing to create an emulsion takes place within the interior of a smooth-walled cylindrical reaction vessel. Welded to the exterior surface is a jacket 30 that is provided for heating/cooling purposes. Because this exterior jacket is referred to as being formed of a plurality of baffles 40, it appears that it has been cited and combined with the references to Schembri and Chung et al. It is submitted that such combination is most clearly one carried out in hindsight and that there is nothing to be found from the shape of a cooling/heating jacket which is welded to the exterior of a large reactor for carrying out a suspension polymerization process, and through which a coolant or heating liquid is being pumped, that would logically reasonably suggest any adaptation of the construction of a microarray hybridization device. Accordingly, it is submitted that the rejection based upon the nonalagous disclosure of del Valle et al. should be reconsidered and withdrawn.

The disclosures of Bedingham et al. U.S. Patent Publication No. 2002/004703 and Taylor et al. PCT International Publication No. WO 99/36576 contain no disclosure with regard to the employment of bubble-fracturing elements that would cause the rupture of a bubble initially present within a liquid confined in a chamber upon manipulation of a microarray hybridization device. Thus, further comment upon these two references is considered to be unnecessary.

New claim 23 finds support in original claim 14 and in FIGS. 1-4 of the drawings. More specifically, it recites that the microarray includes 3D spots in the chamber which is defined by a rectangular perimeter barrier in a region between a flat substrate and a flat cover that contains a filling port through which a liquid target solution can be supplied to such port and means for sealing such port so that the device may be manipulated in a substantially vertical plane about a horizontal axis, as illustrated in FIG. 4 of the drawings and described on page 10. Thus, the claimed subject matter is further distinguished from the circular device of Schembri which uses thermocapillary action to promote movement in a thin film along a circular perimeter while the circular filling port in the cover 11 remains open. The microfluidic mixer and the microfluidic reactor disclosed by Chung et al., which employ continuous flow through chambers, are not truly relevant to a device as defined in new claim 23. Dependent claims 24 and 25 are patterned after original claims 7, 8, 13 and 14.

In view of the foregoing amendments and remarks, it is believed that independent claims 1, 11 and 23 to Applicants' microarray hybridization device should be allowed, along with dependent claims 2-10, 12, 13, 24 and 25, and allowance thereof is respectfully requested. Upon allowance of claim 1, it is submitted that claims 18-22 should be rejoined, and such rejoinder and allowance of claims 18-22 are also respectfully requested.

In view of the foregoing and in the absence of more pertinent prior art, it is submitted that this application should now be in condition for allowance, and such action is courteously solicited.

Respectfully submitted,

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